Claims

Sub C1

1. A method for analysing a sample comprising the steps of:

1. providing a polypeptide pair comprising a first polypeptide and a second polypeptide capable of associating, wherein

2. the association of the polypeptides is detectable, and

3. modification of at least one of the polypeptides results in modulation of the association;

4. immobilising the first polypeptide to a physical support;

5. contacting the immobilised polypeptide with the second polypeptide, and

6. assaying the modification of at least one of the polypeptides by measuring the association of the second polypeptide to the first polypeptide.

2. The method of claim 1 wherein either the immobilised polypeptide or the binding partner polypeptide is associated with a label.

3. The method of claim 2 wherein both the immobilised polypeptide and the binding partner polypeptide are associated with a label.

Sub C2

4. The method of claim 3, wherein said labels on the immobilised and binding partner polypeptides are different.

5. The method of claim 2 or 3, wherein said label comprises a fluorescent label.

Sub C3

6. The method of claim 3 or 4, wherein said detectable signal is generated by an interaction between the labels.

7. The method of claim 6, wherein said interaction comprises energy transfer.

Sub C4

8. The method of claim 1, wherein said association is measured by monitoring the molecular mass of the hybrid species comprising the second polypeptide associated with the first polypeptide.

9 The method of claim 1 or claim 8, wherein said association is measured by surface plasmon resonance.

10. The method of claim 2 or 3, wherein said label comprises a radioactive label.

11. The method of claim 10, wherein said association is measured by scintillation proximity assay.

Sub C5

12. The method of claim 1, wherein said association is measured using an antibody.

13 The method of claim 1, comprising the additional step, prior to sstep (d), of contacting one or both of said first and second polypeptide(s) with an agent capable of modifying one or both of said polypeptides.

14. The method of claim 1, wherein the immobilised polypeptide is the polypeptide which is susceptible to modification.

15. The method of claim 1, wherein said association is measured in real time.

Sub C6

16. The method of claim 1, wherein said assaying said modification of step (d) comprises assaying one of: proteolysis, phosphorylation, acylation, glycosylation, farnesylation, geranylation, ubiquitination, prenylation, sentrinisation, and ADP-ribosylation, or the reversal of any of these modifications.

17. A polypeptide pair comprising a first polypeptide immobilised to a support, and a second polypeptide bound to the first polypeptide, wherein

7. the binding of the polypeptides is detectable, and

8. modification of at least one of the polypeptides results in modulation of the binding.

18. A method for detecting or monitoring the activity of a modulator of a polypeptide modifying agent, comprising the steps of:

providing a first polypeptide, and a second polypeptide, wherein

at least one of the polypeptides is susceptible to modification, and

the first and second polypeptides are capable of binding to each other, and modification of one or both of the polypeptides by the modifying agent results in modulation of the binding of the polypeptides to each other;

allowing the polypeptides to bind to each other,

contacting the polypeptides with a modifying agent,

detecting modulation of the binding of the polypeptides to determine a reference signal modulation,

contacting the polypeptides with a modifying agent and a candidate modulator of the modifying agent, and

detecting modulation of binding of the polypeptides, and comparing the modulation detected with the reference signal modulation.

19. A support comprising one or more immobilised polypeptides, wherein

at least one of the immobilised polypeptides is susceptible to modification, said modification being detectable by a method comprising:

contacting the immobilised polypeptide with a test sample which may contain an agent capable of modifying the immobilised polypeptide;

contacting the immobilised polypeptide with a binding partner polypeptide, wherein the binding of this partner polypeptide to the immobilised polypeptide is at least partly dependent on the modification state of the immobilised polypeptide

measuring the association of the binding partner polypeptide to the immobilised polypeptide.

add C8 → add Fc